NUS Graduate School for Integrative Sciences and Engineering
Research Project Write-up

Title of Project :	MR tracking of stem cells with nanoparticles and genetic modification
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Short Description

Cellular transplants may cure diseases that are otherwise untreatable by directly replacing defective cells or creating a therapeutic environment by paracrine mechanism. A method of identifying, tracking and monitoring the location of transplanted cells, serially and non-invasive is essential to the development of cellular therapy, as a gauge of efficacy and safety. Magnetic resonance imaging (MRI), when coupled with MR-visible cellular labels, provides the required resolution, sensitivity and penetration depth for in vivo tracking of cells. The most useful labels for this purpose are magnetic nanoparticles that cells can be encouraged to engulf.

Recent attention has been focused upon the safety of these nanoparticles. Depending on the labelling conditions, nanoparticles can usually reside for days in the cytoplasm without deleterious effects. However, there have been a few reports on the nanoparticle inhibition of cellular function or the reduction in viability of cells post-transplantion. The critical question on long term safety of these nanoparticles has never been addressed.

In order to study the safety aspects of nanoparticles, we will be utilizing:

1. Electron microscopy to study the mechanism of nanoparticle uptake by mesenchymal stem cells;
2. apoptotic, differentiation and surface epitpe assays to delineate long term viability and cellular function after nanoparticle labeling;
3. epigenetic assays to define whether interactions of nanoparticles will lead to alterations in methylation and histone configurations.

Other studies will focus on in vivo tracking studies of different primary human stem cells such as mesenchymal stem cells, neural stem cells and endothelial progenitor cell types labeled either with iron-oxide nanoparticles, or through viral transduction with a ferritin or transferring transgene. Cellular tracking will be done in appropriate injury model, where transplanted cells will be imaged longitudinally, and confirmed through terminal necropsies.

Through this project, the candidate will have exposure and involvement in a multitude of technologies

1. The isolation, characterization and application of primary human stem cells
2. The synthesis or manipulation of biocompatible, magnetic nanoparticles

3. Application of lentiviral vectors for stable gene transfer
4. Animal models of tissue injury, xenogeneic cellular transplantation work and subsequent histological and molecular anlaysis.
5. Confocal microscopy, electron microscopy and MRI